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Promoting Sleep: Adapting to Shiftwork and Time Zone Change

Barbara M Stone
Centre for Human Sciences, Defence Evaluation and Research Agency
Bldg F138, Protection and Performance Dept.
Farnborough, Hampshire, GU14 0LX, United Kingdom

INTRODUCTION

The changes in performance that arise in shiftworkers and after transmeridian flights can be attributed, at least in part, to the reduction in both the quality and quantity of sleep which occurs as a result of disruption of the normal pattern of sleep and wakefulness. Sleep disturbance associated with shiftwork is well documented (1-4). Sleep during the day is shorter and more disturbed than sleep at night, and it has been estimated that, by the end of a week of night duty, the equivalent of at least one night's sleep may have been lost (5). While the duration of slow-wave sleep is unchanged following the night shift, due to prior wakefulness, stage 2 and rapid eye movement (REM) sleep are reduced. Further, in shiftworkers over about 40 years old, the usual decline in sleep quality and quantity with increasing age exacerbates the problems associated with an unusual pattern of work and rest (6-8). This age-related difference in sleep is also evident in studies of transmeridian travel (9).

There have been many studies of sleep after transmeridian flights. In general, the severity of sleep disturbance following a time zone change is dependent upon the direction of travel and the number of time zones crossed, and is influenced by the timing of the flight itself (10-12). After an eastward journey, when sleep is scheduled in advance of the "home" bedtime, difficulty in falling asleep may be accompanied by increased wakefulness in the early part of the night, though these changes may not be apparent on the first night in the new time zone if the flight involves overnight travel without sleep. Problems with sleep may continue for several days after the flight, with reductions in REM sleep and possibly slow-wave sleep, and this may be followed by a compensatory increase in REM sleep several nights later. Sleep disturbance after a westward flight is usually less persistent, lasting perhaps 2 or 3 days. Sleep is likely to be of good quality in the early part of the night, with increased slow-wave activity on the first night due to the delay to the first rest period. On subsequent nights, when the pressure for slow-wave sleep is less, there may be an increase in REM sleep as bedtime corresponds with early morning in the "home" time zone, when REM sleep predominates and body temperature begins to rise (13,14). Awakenings may be evident towards the end of the night at the time corresponding to daytime in the "home" time zone.

Given the adverse effects of sleep loss on alertness, one approach to optimizing performance in situations involving shiftwork or transmeridian flights is to preserve sleep as much as possible. This can be approached in two ways: first, by the application of sleep-promoting techniques and by attention to the circumstances which surround sleep; and second by the use of hypnotic substances. Sleep may, of course, be improved by changing duty schedules or resetting the body clock, but these techniques are outside the scope of this paper.

Paper presented at the RTO HFM Workshop on "Individual Differences in the Adaptability to Irregular Rest-Work Rhythms/Status of the Use of Drugs in Sleep-Wakefulness Management", held in Venice, Italy, 3-4 June 1999, and published in RTO MP-31.

TECHNIQUES TO IMPROVE SLEEP

Among the techniques or strategies that may be applied to promote sleep are those which aim to ensure that the sleeping environment is optimal. While it is true that shiftworkers sleep badly even in sound- and light-proofed accommodation (15), sleep will be more disturbed if the environment is noisy and light. Similarly, after transmeridian flight, it is important to ensure that extraneous noise and light are kept to a minimum to alleviate problems related to staying asleep in the morning or to falling asleep at night. If the sleeping environment is not ideal, earplugs and eyeshades can be used to screen unwanted external stimuli. These strategies are frequently used by airline pilots sleeping in hotel accommodation or when they have to obtain rest in the bunk facilities on board the aircraft itself on long-range flights (9). Aromatherapy products have also been promoted for the treatment of jet lag and sleep disturbance.

Caffeine (Fig 1) and alcohol are known to have detrimental effects on sleep (16,17) though alcohol may initially promote sleep onset. Avoidance of caffeine close to bedtime and of excessive alcohol intake are measures that will serve to improve the sleep of shiftworkers and intercontinental travellers. The influence of dietary constituents has also been considered, and it has been suggested that a "jet lag diet" will speed adaptation of sleep and other rhythms (18). This diet proposes that an evening meal rich in carbohydrates will provide a source of tryptophan for serotonin synthesis to assist sleep, and that protein-rich meals in the morning will provide tyrosine to enhance catecholamine levels and increase alertness during the day. However, a review of this field of research concluded that there was no evidence to support this approach (19). Administration of tryptophan has been reported to increase total sleep time on the first night after transmeridian travel westward (20), though its effects on sleep are limited (21)

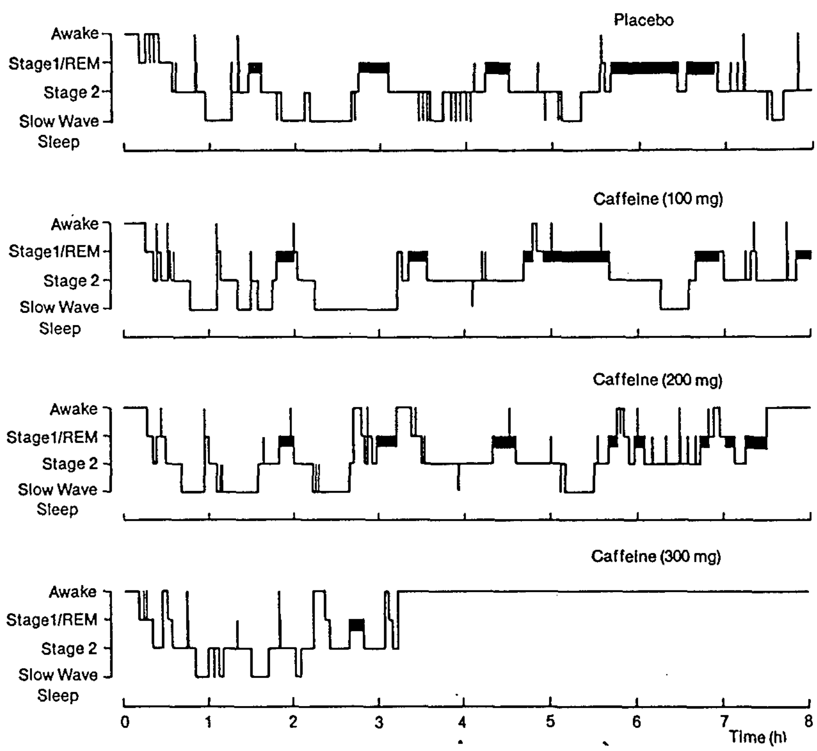

Fig 1 Effect of caffeine (100, 200 & 300mg) on sleep in a normal subject.

Changes in the timing of rest periods and naps during shiftwork or after a time zone change can lead to improvements in sleep. However, it is necessary to balance the changeover times of shifts as sleep duration is reduced if the morning shift starts early or if the night shift finishes late (22). During transmeridian travel, if it is not possible to sleep during an overnight eastward flight, restricting sleep on arrival can aid sleep on the first night and, possibly, speed the rate of adaptation. If passengers are able to sleep on board the aircraft, then sleep coinciding with bedtime in the destination time zone will avoid the desire for a sleep on arrival and is likely to lead to better-quality nocturnal sleep. Conversely, sleeping at a time coinciding with night-time in the home time zone may lead to disturbed sleep at the destination and, possibly, delayed adaptation.

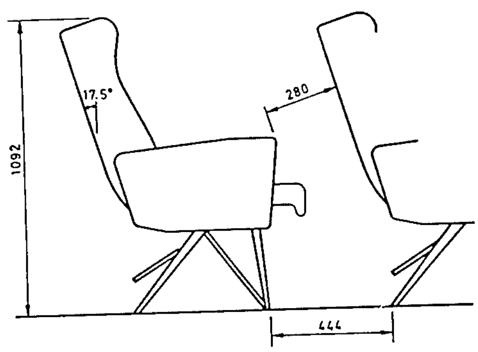

Fig 2 Armchair. The back angle with the verticale is 17.5°. but there is no rest for the legs or feet.

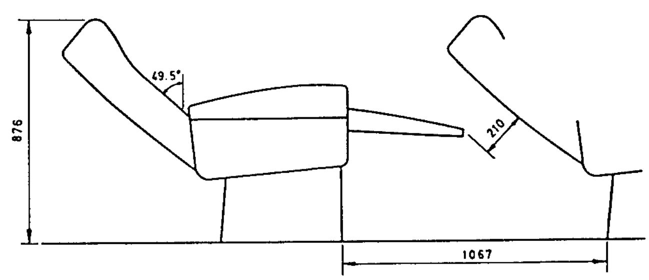

Fig 3 Sleeperette. The back angle with the vertical is 49.5°, and the rest provides horizontal support for the legs.

Finally, sleeping position is also important, and particularly relevant to long-haul air travel (Figs 2, 3 & 4). Passengers on board aircraft are required to adopt a posture that may make sleeping difficult. Near-horizontal sleeping facilities are preferable, but they are at present limited. Assessment of sleep quality in aircraft seats has shown that the greater the back angle from the vertical, the more likely it is that the passenger will obtain reasonable sleep. Adequate sleep is likely as long as the back angle is around 40 degrees (23). Over the last few years there have been many improvements including full sleeping facilities.

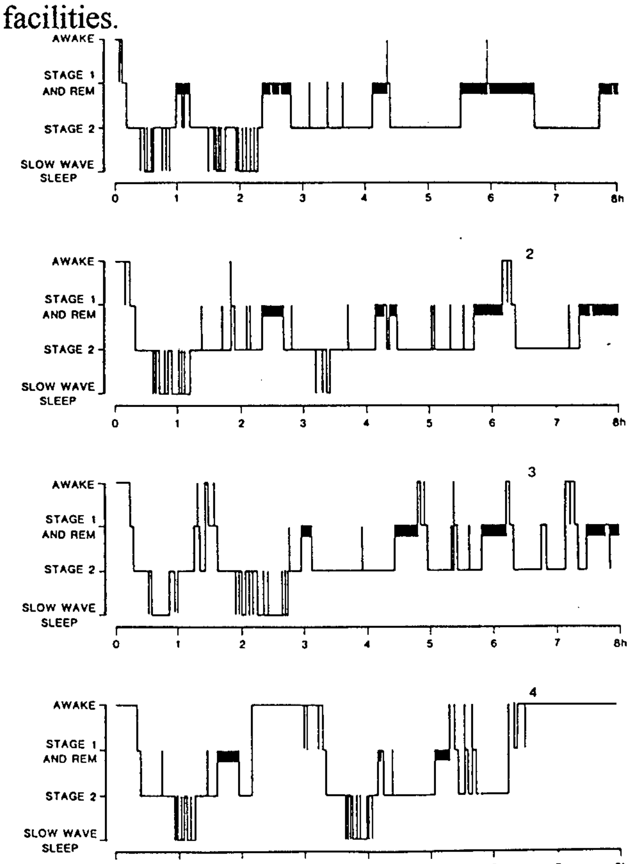

Fig 4 Hypnogram for a subject in bed (1), and on the sleeperette (2), reclining seat (3) and armchair (4). Sleep was markedly disturbed in the armchair with an hour period of wakefulness, and shortened sleep. Sleep in the reclining seat also showed some disturbance, with more awakenings particularly during the latter part of the night.

HYPNOTIC DRUGS AND SLEEP-PROMOTING SUBSTANCES

The second approach to preserving sleep involves the use of drugs. The largest class of hypnotics, the benzodiazepines, is known to speed sleep onset, reduce awakenings, and increase total sleep time in normal sleepers and in those suffering from transient and chronic insomnia. However, they may delay the appearance of REM sleep, reduce slow-wave sleep, and enhance sleep spindles (24-27). Imidazopyridine, zolpidem, and the cyclopyrrolone, zopiclone, have similar effects on the EEG as benzodiazepines (28,29). Zolpidem, however, may increase slow-wave sleep (Fig 5), at least in young individuals (29,30), and there may be a moderate increase in slow-wave sleep with zopiclone (31).

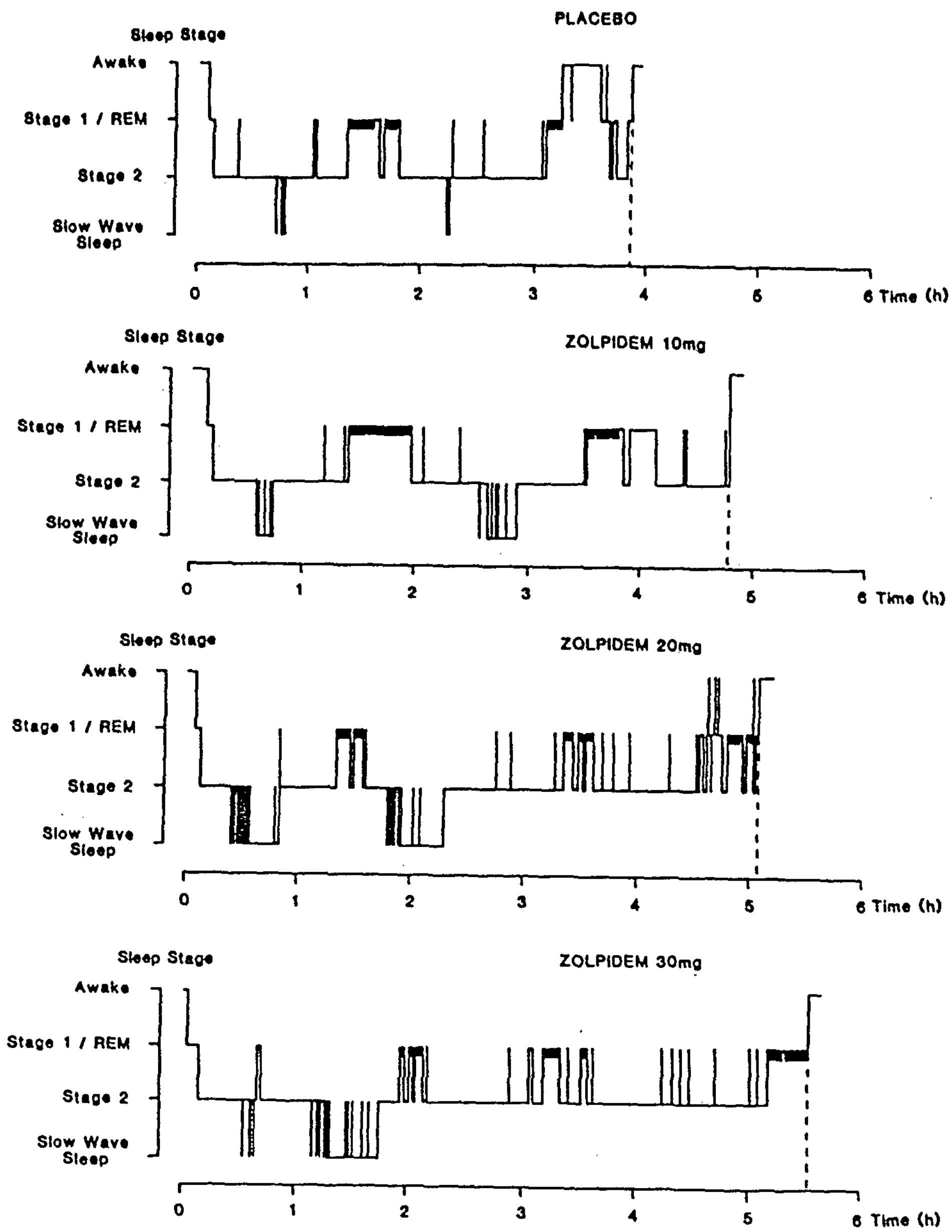

Fig 5 Daytime sleep patterns of a young adult after ingestion of placebo and 10, 20 and 30mg zolpidem. Wakefulness was reduced with zolpidem and sleep period time was increased. With 20 and 30mg there was an increase in the duration of slow wave sleep and total sleep time.

While a hypnotic should, ideally, accelerate sleep onset and sustain sleep for a useful period of time, and while it may be desirable to preserve slow-wave sleep, the overriding factor when considering the potential use of a hypnotic by shiftworkers or during and/or after transmeridian flights is the drug's duration of action (32). Active metabolites may also prolong the duration of action of a particular drug. Clearly, the benefits associated with improved sleep may well be offset if the hypnotic leads to unwanted effects on alertness after the rest period. An hypnotic that is rapidly cleared and is without active metabolites, is likely to be free of residual effects and without accumulation if taken daily. However, it must be appreciated that clearance is dependent on absorption, distribution and elimination, and all these factors must be taken into consideration when duration of action is being determined. Drugs with appropriate pharmacokinetic profiles have been evaluated in simulated and field studies of shiftwork and jet lag. In such situations, hypnotics are likely to be effective due to their sleep-promoting properties rather than any effect on circadian rhythms.

TRANSMERIDIAN TRAVEL

Hypnotics with a limited duration of action may be useful during the adaptation phase after a transmeridian flight. For example, temazepam taken during eastward and westward flights across 11 time zones at the time corresponding to bedtime in the destination time zone and for 4 days after arrival improved subjectively assessed sleep without affecting performance during the day (33). In another study brotizolam reduced wakefulness and increased stage 2 sleep on the first 2 nights after a 5h westward time zone change (Fig 6) and the drug was also effective in reducing wakefulness and stage 1 sleep for 5 nights after the eastward journey (10) (Fig 7). Improvements in sleep continuity with hypnotics several days after an eastward flight may be accompanied by a reduction in REM sleep on those nights when an increase is observed with placebo (12).

However, the effects depend on the extent of sleep disturbance, which, in turn, depends on the direction of travel, number of time zones crossed, and the age of the individual. For example, the short-acting hypnotic midazolam, taken for 4 nights after a 7h time zone change, improved sleep, though only after the eastward flight on the first and third night when sleep with placebo was poor (34). Similarly, on the first night after an eastward flight when sleep after placebo was better than control due to considerable sleep loss, it was not possible to show a further improvement in sleep with brotizolam (10).

In addition to using hypnotic drugs on arrival in a new time zone, passengers may consider using medication on the flight itself to assist sleep timed to coincide with the nocturnal rest period at their destination. In an unfavourable environment simulating troop transportation, the hypnotics triazolam and zolpidem, with elimination half lives of between 1.5 and 2h, had comparable sleep-promoting properties (35). However, a field study suggested that triazolam may be ineffective on board an aircraft if there is no control over factors such as the timing of meals or the cabin lighting (36). Indeed, to sustain sleep during a long flight, a hypnotic with less rapid clearance may be more appropriate.

In a laboratory study of sleep in airline seats, though midazolam and brotizolam improved sleep, midazolam further suppressed REM sleep to below levels that were already reduced by sleeping in the seat (37). An additional consideration of taking a high dose of a rapidly eliminated hypnotic is the possibility that high plasma levels may impair performance in an emergency situation (35) or on arrival at the destination

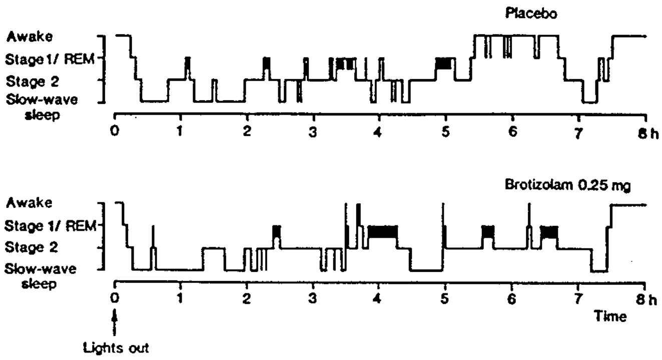

Fig 6 Sleep patterns of an individual on the first night after a 5h westward time zone change after placebo and brotizolam ingestion at lights out (13).

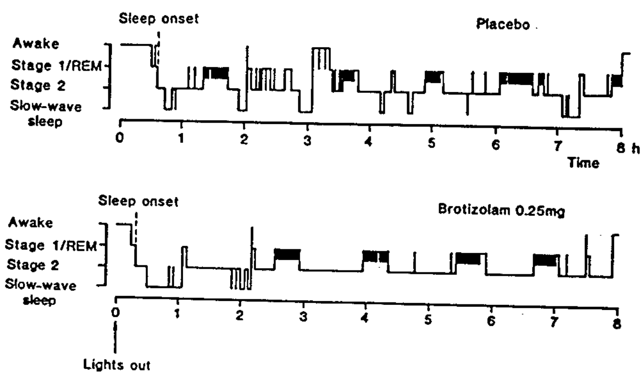

Fig 7 Sleep patterns of an individual on the fourth night after a 5h eastward time zone change after placebo and brotizolam ingestion at lights out (13).

(36), and there could be rebound effects on sleep parameters during the next rest period.

Melatonin has been reported to improve the subjective adverse effects of jet lag in a number of studies (38-42), though some of these studies have shown no effect on measures of sleep duration. In one study of military personnel following an 8 hour eastward time zone shift 10mg melatonin was reported to advance the timing of sleep and increase sleep duration measured by actigraphy (42). There have, however, been reports of sleep difficulties after melatonin (5mg) use in the treatment of jet lag (41). Sleep fragmentation with melatonin (5mg) has also been observed in laboratory studies (43). The only sleep EEG data relates to laboratory studies of simulated change using 5mg melatonin. This showed some increases in sleep duration and efficiency in the first night after the phase shift, but also reductions in slow wave sleep (44).

SHIFTWORK

Hypnotics may also be used by shiftworkers, and a recent review (45) concluded that hypnotics improve daytime sleep by increasing sleep efficiency and duration. Interestingly, the efficacy of hypnotics for nocturnal sleep may not always predict their effectiveness for daytime sleep. With this in mind, evaluation of new compounds should include assessment of sleep-promoting properties at the relevant times of the day. Such studies would also take account of the further, different sleep problems experienced by shiftworkers in relation to their different schedules. As far as the night shiftworker is concerned, sleep onset is not likely to be as much of a problem as sustaining sleep during the day, whereas those working an early-morning shift who choose to retire to bed in the early evening may have difficulty falling asleep.

To date, the majority of studies on hypnotics and shiftwork have been laboratory-based simulations. In these situations the effects of cumulative sleep loss may be underestimated when using subjects who are not shiftworkers, particularly if they are young adults who are normally good sleepers. In addition, sleep is more likely to be sustained when environmental conditions are controlled. For example, triazolam was more effective in sustaining daytime sleep in middle-aged shiftworkers who slept in the laboratory (46) than in middle-aged individuals who slept at home (47).

Studies suggest that the less restful sleep of the middle-aged is more likely to be improved by hypnotics than the sleep of young adults (30,48), and older shiftworkers have reported greater use of sleeping pills than their younger colleagues (8,49). Furthermore, it is possible that middle-aged individuals may derive greater benefit from hypnotics in terms of improved alertness overnight (47,48) than young adults. Indeed, for young subjects who are good sleepers there may be no difference in overnight performance following a drug-assisted or natural evening sleep (50).

Another factor to consider is the potential effects of withdrawal of medication. Withdrawal of triazolam after 4 days for daytime sleep led to a greater reduction in sleep efficiency in middle aged individuals than young adults (48), though the rebound effects may have been related to the high dose used (0.5mg). Indeed, this dose of trazolam has been shown to impair performance following daytime sleep (46), overnight sleep (51), and both sleep on board aircraft (37) and in conditions simulating those on board aircraft (36). While a lower dose of triazolam (0.25mg) has been shown to improve subjectively assessed sleep without having residual sequelae in military shiftworkers with disturbed sleep (52), other studies suggest that low doses of hypnotics may not be effective in some middle-aged individuals (47,53,54).

It is important to balance the requirement to improve sleep with the need to avoid residual effects. Zolpidem has a pharmacokinetic profile similar to triazolam (32) and, though it would appear to be free of residual effects, improvements in daytime sleep were only observed at relatively high doses (20-30mg) in young adults and were accompanied by a reduction in REM sleep (30). While zolpidem may be more effective in poor sleepers a sufficiently long duration of action is important in sustaining daytime sleep. For example, temazepam has been used successfully in doses of 10-20mg by military aircrew to assist sleep at unusual times of the day during intensive operations when the interval between drug ingestion and commencement of duty may be as short as 6h (55,56). Similarly, temazepam improved daytime sleep and increased alertness during a simulated night shift (57). Zopiclone may be an equally effective hypnotic as it improved sleep when bedtime was advanced by 4h (58) and when advanced or delayed by 6h (59). Decrements in performance some 9h after drug ingestion have been reported (35), and a recent review of its residual effects has indicated caution in its use in critical situations (60).

There have been two field studies which have investigated the use of melatonin to assist adaptation to shiftwork, though only one of these monitored sleep (61,62). A 5mg dose prior to daytime sleep during a period of 7 consecutive night shifts was reported to improve sleep quality and quantity assessed subjectively. In a study simulating night shiftwork, melatonin was reported to improve daytime sleep quality as measured by actigraphy (63).

CONCLUSION

In summary, management of sleep disturbance arising from shiftwork and transmeridian travel should be approached by attention to sleep hygiene, including factors such as sleep timing, environmental conditions, and restriction of "social" drugs. However, the successful application of such measures is not well documented. If such an approach is ineffective and due attention has been given to optimizing duty schedules then the occasional use of an hypnotic free from residual effects and of accumulation on daily ingestion may be indicated. The lowest effective dose should be used and the concomitant use of alcohol avoided or restricted.

Studies reporting beneficial effects of melatonin in the treatment of jet lag have largely been based on subjective assessments, with only two studies monitoring physiological rhythms. There is some evidence from laboratory investigations that melatonin does have circadian phase shifting properties, but there is litte or no information available on the effect of melatonin upon objective measures of performance and sleep in the field. In the laboratory the observed effects of melatonin on sleep have been inconsistent.

Advice on the use of hypnotics requires further clarification, particularly for those individuals with poor sleep who frequently undertake night shiftwork or regularly cross time zones. The potential users should be aware of the general recommendation that hypnotics should only be taken occasionally. For example, this could involve using a suitable hypnotic on alternate days at the start of a period of nightwork, so that a sleep deficit does not accumulate. Dissemination of current knowledge and guidelines on promoting sleep to occupational physicians, shiftworkers, and transmeridian travellers should be encouraged. At present, however, there is little information on the pattern of hypnotic usage and efficacy in shiftworkers over time. Further research in this area, including feedback from users, would allow better definition of the most suitable treatments.

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